The impact of local heterogeneity on alternative control strategies for foot-and-mouth disease

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The 2001 epidemic of foot-and-mouth disease (FMD) in the UK resulted in the death of nearly 10 million livestock at a cost that was estimated to be up to £8 billion. Owing to the controversy surrounding the epidemic, the question of whether or not alternative policies would have resulted in significantly better control of the epidemic remains of great interest. A hexagonal lattice simulation of FMD in Cumbria is used to address the central question of whether or not better use could have been made of expert knowledge of FMD transmission to target pre-emptive culling, by assuming that the premises at greatest risk of becoming infected can be targeted for culling. The 2000 UK census and the epidemiological database collected during the epidemic are used to describe key characteristics of disease transmission, and the model is fit to the epidemic time-series. Under the assumptions of the model, the parameters that best fit the epidemic in Cumbria indicate that a policy based on expert knowledge would have exacerbated the epidemic compared with the policy as implemented. However, targeting more distant, high-risk farms could be more valuable under different epidemic conditions, notably, if risk factors of sufficient magnitude could be identified to aid in prioritizing vaccination or culling of farms at high risk of becoming infected.

Keywords: model; spatial; simulation; lattice; culling; vaccination

1. INTRODUCTION

In the UK, emergency vaccination has been recommended to control future large outbreaks of foot-and-mouth disease, or FMD (Byrne 2002; Follett *et al.* 2002), in part owing to the continued controversy over the 2001 epidemic and the extent of the slaughter that resulted. In particular, a major criticism has been a lack of sufficient veterinary input into decision-making (Anon. 2002; Cunningham *et al.* 2002; Gill *et al.* 2002). Previous reports (Ferguson *et al.* 2001*a*,*b*; Keeling *et al.* 2001) have described the mathematical models used to advise control policies during the epidemic. However, they have not addressed the central issue of whether prioritizing the cull of premises at risk owing to proximity to infected premises, or IPs (the 'contiguous' or CP cull), compromised efforts to trace and cull 'dangerous contacts' (DCs) that would have more efficiently controlled the epidemic. By assuming that premises' susceptibility is randomly distributed, the effect of culling highly susceptible and preclinical IPs as DCs is examined. Using this approach to examine the large Cumbrian epidemic, simulations show that even with generous assumptions regarding ascertainment of disease transmission risk, prioritizing DC culling would not have changed its course. Whether such knowledge could benefit culling and/or emergency vaccination policies in the future depends on how soon it is available, and how strong is the differentiation between infected and uninfected premises. Earlier decision points and broader variability are therefore examined, as a guide to control policy in future large-scale FMD epidemics. Whereas earlier analyses have indicated that it would have been difficult to mobilize sufficient resources with enough speed to make mass vaccination feasible (Ferguson *et al.* 2001*a*; Keeling *et al.* 2001), anticipation of imminent scientific advances and changes in European Union policy have resulted in the more recent recommendations in favour of emergency vaccination to control large outbreaks. Thus, although a more complete discussion of FMD vaccination issues can be found elsewhere (see Keeling *et al.* 2003), targeting of high-risk farms in an emergency 'ring' vaccination of farms surrounding IPs is examined here.

2. MATERIAL AND METHODS

A prior model of FMD transmission on a hexagonal lattice of farming premises (Kao 2001) is here modified to incorporate the epidemiological data from the 2001 epidemic (as described in Gibbens *et al.* (2001)) and demographic data from the annual agricultural census (UK Ministry of Agriculture 2001) in a more realistic fashion. To consider the impact of local heterogeneity, each premises is assigned a random risk factor that abstractly represents all non-species-dependent variability (differences in biosecurity implementation, local geography, etc.) and modifies the transmissibility of IPs and susceptibility on uninfected premises. It is assumed that DC culling identifies high-risk farms. Owing to the difficulty of detecting FMD in sheep (Hughes *et al.* 2002), it is assumed that only a proportion of infected flocks are detected, with probability 'f'. The remaining infected flocks are only removed owing to the presence of infected cattle on the same premises, or as non-IP culls.

All premises are assigned a location on a hexagonal lattice, with premises at 1 or 0 hex distance considered to be contiguous. One hex is 1.2 km wide; at this scale, each premises has on average six premises within one hex of it, and each occupied hex contains 1.75 premises, on average. Though in some cases this probably overestimates the numbers of 'true' CPs (i.e. where animals and not just addresses or parcels of land are in close proximity), simulations where the number of neighbours is restricted to six (as in Kao 2001) show no significant difference in fit to the epidemic dynamics, and the assumption used better reflects the actual distribution of CP culls per IP.
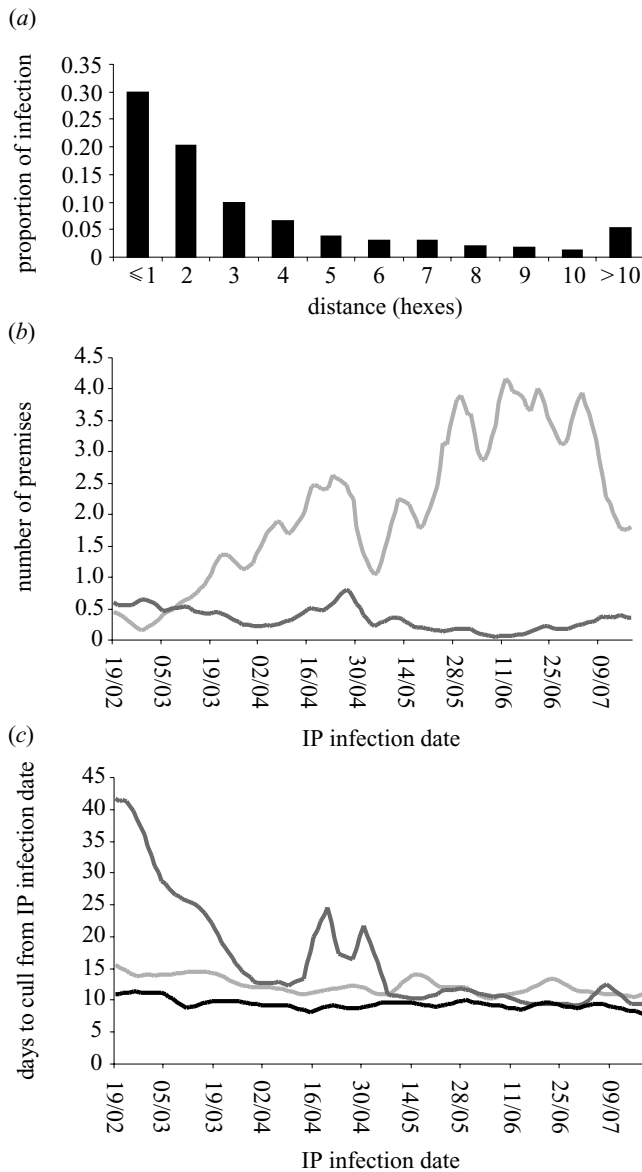
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(a)

(b)

(c)

Figure 1. Simulation parameters, estimated directly from the epidemiological databases as described in Gibbens *et al.* (2001). (*a*) Transmission kernel. Transmission at greater than 10 hex is assumed to occur at a random location. (*b*) Moving weekly average of the number of DC culls (dark grey) and CP culls (light grey) per IP throughout the first 150 days of the epidemic (fixed thereafter). (*c*) Moving weekly average of the time to cull IPs (black), DCs (dark grey) and CPs (light grey) from the estimated infection date of the source IP.

Premises' status (including day of infection, day of culling and numbers of cattle and sheep per premises) is updated daily. Clinical signs are assumed to be visible 7 days after the day of infection. The daily probability p_i that a susceptible farm i will become infected is

$$p_i = 1 - \prod_{j \in \text{IPs}} \left\{ 1 - \frac{R_0}{6} \times \Delta(t_j) K(d_{ij}) \theta_i \tau_j r_i r_j \right\},$$

where $\Delta(t_j)$ is the proportion of infectiousness on day t_j post-infection for IP j, $K(d_{ij})$ is the transmission kernel (calculated from IPs with identified links to source IPs) at distance d_{ij}, and r_i is the random risk factor for i. The distribution of risk is assumed to be log-normal, with a mean of 1. The parameters θ_i

and τ_j are the susceptibility and transmissibility of premises i and j, respectively, defined (from Keeling *et al.* (2001)) to be proportionate to the number of cattle and sheep, according to the relationships

$$\theta_i \propto 15.1 \times n_i^{\text{cattle}} + n_i^{\text{sheep}}$$

$$\tau_i \propto 1.82 \times n_i^{\text{cattle}} + n_i^{\text{sheep}}.$$

The actual values are normalized so that, on average, θ_i and τ_j are equal to 1. A new IP j has a probability of being removed as a DC cull of

$$p_{\text{DC\_kill}} = \frac{n_{\text{DC}}(t)}{R_0} \times X \times r_j,$$

where $n_{\text{DC}}(t)$ is the number of DC culls triggered by an IP infected on day t, and $X(t)$ is the quality of the DC cull (i.e. the probability that epidemiological tracing will find a pre-clinical IP, or a premises at high risk of infection). For $X(t)$ near 1, this slightly underestimates the proportion of DC culls, because each IP will typically infect, on average, fewer than R_0 premises once the epidemic has started, but in practice the difference is slight. DC culls that do not remove IPs and all other non-IP culls remove premises at random from a list of the most probable culls. The probability of culling premises i is given by

$$p_i = 1 - \prod_{j \in \text{IPs}} (1 - C(i, d_{ij})),$$

where $C(i, d_{ij})$ is the 'culling kernel', a weighting function for the probability of being culled based on the distance d_{ij} from the triggering IP, and the characteristics of premises i. For the CP cull,

$$C(i, d_{ij}) = \begin{cases} 0, & d_{ij} > 1, \\ \dfrac{c(t)}{N_i}, & d_{ij} \leq 1, \end{cases}$$

where N_i is the number of premises contiguous to i. For DC culls,

$$C(i, d_{ij}) = \begin{cases} X(t), & j \in D \quad N(D) = \dfrac{c(t)}{X}, \\ 0 & \text{otherwise}, \end{cases}$$

where $c(t)$ is the average number of culls triggered by an IP detected at time t (specific for each culling policy) and D is the set of the $N(D)$ premises most susceptible to infection from i. If a premises has been infected by i but is as yet undetected, then it takes precedence for culling over more susceptible, uninfected premises. For example, if an IP infects one other premises, if the number of DC culls is $c(t) = 2$ and if the culling success is $X = 0.25$, then the eight most likely premises to have been infected (the new IP and the seven premises with the highest susceptibility) will be removed as DC culls with 25% probability. In addition, the Cumbria-specific policy of culling all pigs and sheep on premises within 3 km of an IP (the 3 km cull) affects premises within a 3 hex distance. The 3 km cull probability is fit to the data using an exponential ($C(i, d_{ij}) = 0.21 \exp(-0.167 d_{ij})$, $R^2 = 0.95$). Any premises culled for more than one reason are slaughtered at the earliest calculated date. Times to slaughter for all types of cull, and the number of CP and DC culls per IP, were based on weekly moving averages of slaughter statistics from the epidemiological database (Gibbens *et al.* 2001), and are shown in figure 1.
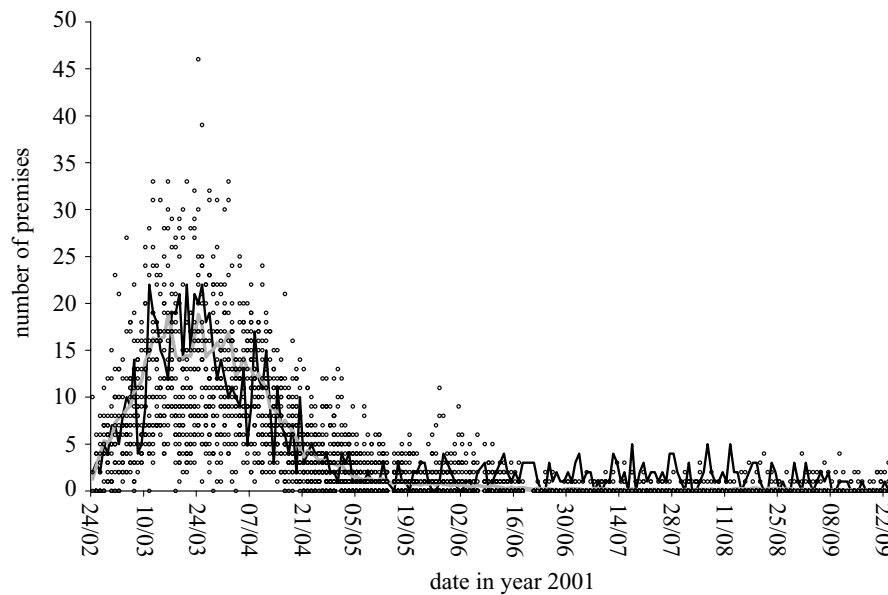
Figure 2. Temporal representation of the epidemic in Cumbria. The black line represents the true epidemic incidence, based on estimated infection dates from the FMD database. The grey line is the mean incidence over 100 simulations. The circles are the data points from 50 simulations.

To examine targeted vaccination, a fixed proportion of farms in a 3 hex ring (3.6 km radius) surrounding each IP are vaccinated, under the assumption that premises can be prioritized in a fashion similar to DCs. For existing FMD vaccines, protective titres of antibody have been shown 2–3 days post vaccination, although maximum titres typically are reached at 7–10 days (Woolhouse *et al.* 1996). It is assumed that a vaccine is fully effective 4 days post inoculation, with no prior protection (Doel 1999), and that an adequate diagnostic test is available rapidly to distinguish vaccinated from infected animals. IP and DC culling occur at the same level as occurred in the epidemic, but no other culling occurs.

For a given distribution for r, the basic reproduction ratio (R_0) or the average number of premises that an IP would infect over its lifetime in a completely susceptible neighbourhood (Anderson & May 1992) was estimated by the least-squares best-fit to the time-series of the epidemic from the imposition of movement restrictions on 23 February, to the announcement of the 3 km cull on 23 March. Simulations show that the fit of R_0 is not sensitive to other estimated parameters. To choose the remaining fitted parameters (comparing all combinations of the susceptibility standard deviation $\sigma = 0.25, 0.5, 1.0, 2.0$, $f = 0.1$, 0.2, 0.5, 0.8 and $X = 0.2, 0.5, 0.8$), 200 iterations of the simulation were then run over the length of the actual epidemic in Cumbria (219 days) for each set, and the total number of IPs and culled premises compared with the true epidemic. For a given R_0, several parameter sets were not significantly different at the 95% confidence level. The baseline parameter set ($R_0 = 2.1$, $\sigma = 0.5$, $f = 0.5$, $X = 0.5$) was chosen as the one also best fitting the true epidemic length (105 out of 200 simulations persisting into the last week of the simulation). All simulations were run in MATHEMATICA v. 4.0.

3. RESULTS

In figure 2, the time course of the simulation is compared with the true epidemic in Cumbria. The main course of the epidemic is well reproduced. Simulation incidence in the epidemic tail is low (true epidemic,

1.35 ± 0.22 IPs per day over the last 100 days, versus 0.28 ± 0.01 for the simulations), resulting in an underestimate of the total number of IPs in the epidemic. However, four out of 200 simulations did show incidences of greater than 1, consistent with the true epidemic. The average spatial distribution of IPs over 100 simulations and the spatial distribution of IPs in the true epidemic are shown in figure 3. The distribution is generally consistent; however, it is difficult to compare the true spatial epidemic distribution with the average of simulations because the true epidemic is equivalent to running a single simulation, and when the variation in potential epidemic outcomes is large, it is unlikely that any single simulation would be representative. Qualitatively, there appear to be some potential discrepancies, most notably near the sources of the epidemic, where simulation prevalence appears slightly high.

In figure 4, the baseline scenario is compared with a policy where DC culling is assumed to be highly effective ($X = 1.0$) and is therefore prioritized, with DC culls replacing CP culls with the same report-to-slaughter times, and on a one-to-one basis. Whereas proximity to IPs was recognized as a risk factor from the start of the epidemic, it was only on 29 March that prioritization of CP culling was announced (Anon. 2001). Figure 4*a* shows that, surprisingly, even when prioritized DC culling occurs as soon as 7 days after movement controls were announced (2 March), it is inferior to the CP cull policy. For the variability in r used, the average ratio between r for IPs and susceptible premises over the course of the epidemic is 1.6. This is a consequence of the relatively low variability assumed; alternative simulations with greater heterogeneity ($\sigma = 1.0$, $R_0 = 2.725$) show DC culling to be significantly superior for prioritized DC culling as late as 21 days after movement controls were implemented (16 March, figure 4*b*). In this case, the ratio of r values was 3.0, indicating that, should it be possible to identify factors that influence susceptibility, only very strong dependence on a risk factor or combination of
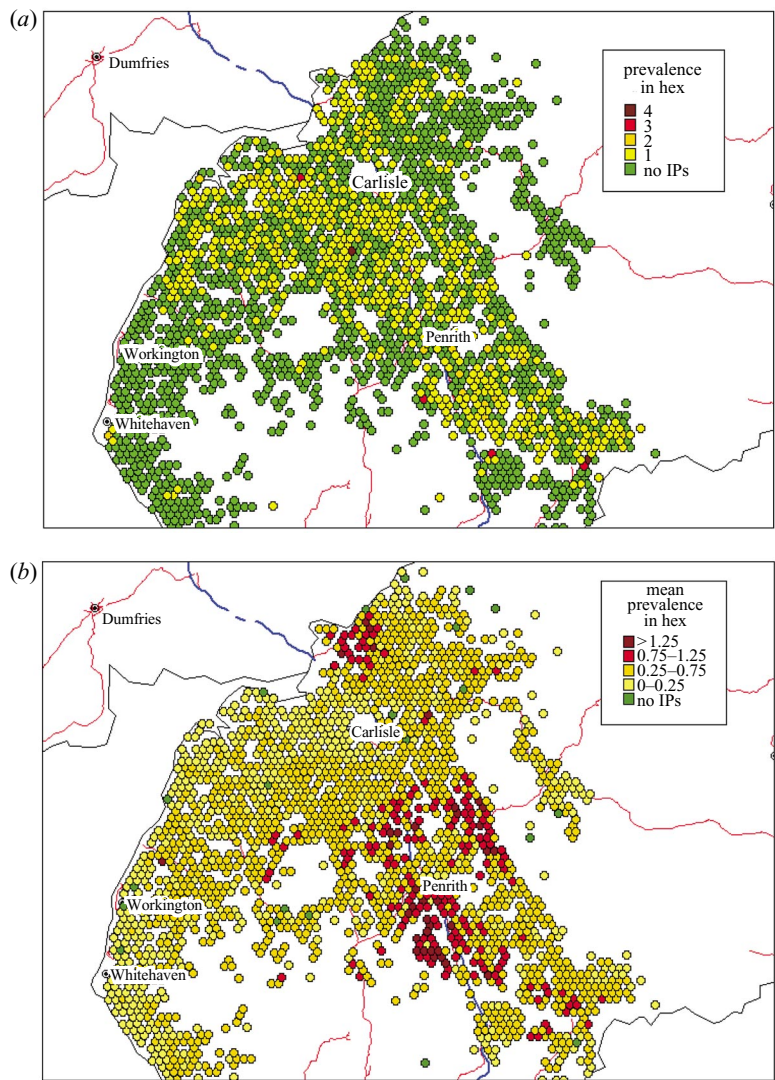
Figure 3. Spatial representation of the epidemic in Cumbria. (*a*) The locations of all IPs, as indicated in the FMD database. (*b*) The average prevalence per hex over 100 simulations for the baseline scenario. Because the FMD database records the location of infected animals to within 1 km, and the agricultural census records only the location of the farm holding, there are some discrepancies in premises locations between the two.
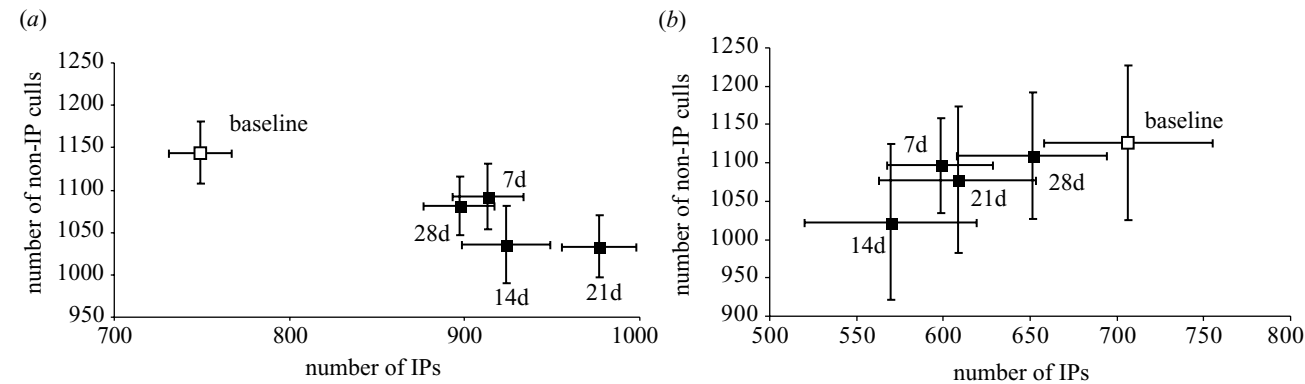

Figure 4. Comparison of DC culling policy versus the baseline policy. Baseline policy in white, prioritized DC culling 7 days, 14 days, 21 days and 28 days after movement controls were initiated on 23 February, in black. DC culls are targeted, with the premises most likely to be infected under the current conditions removed first. Comparison for $\sigma = 0.5$ (figure 3*a*) shows that all alternative policies result in significantly more IP culls, and similar non-IP culls to the baseline scenario. By contrast, for greater variability ($\sigma = 1.0$, figure 3*b*), DC culling appears to be superior. (*a*) Prioritized DC culling versus CP culling: low variability, (*b*) prioritized DC culling versus CP culling: high variability.
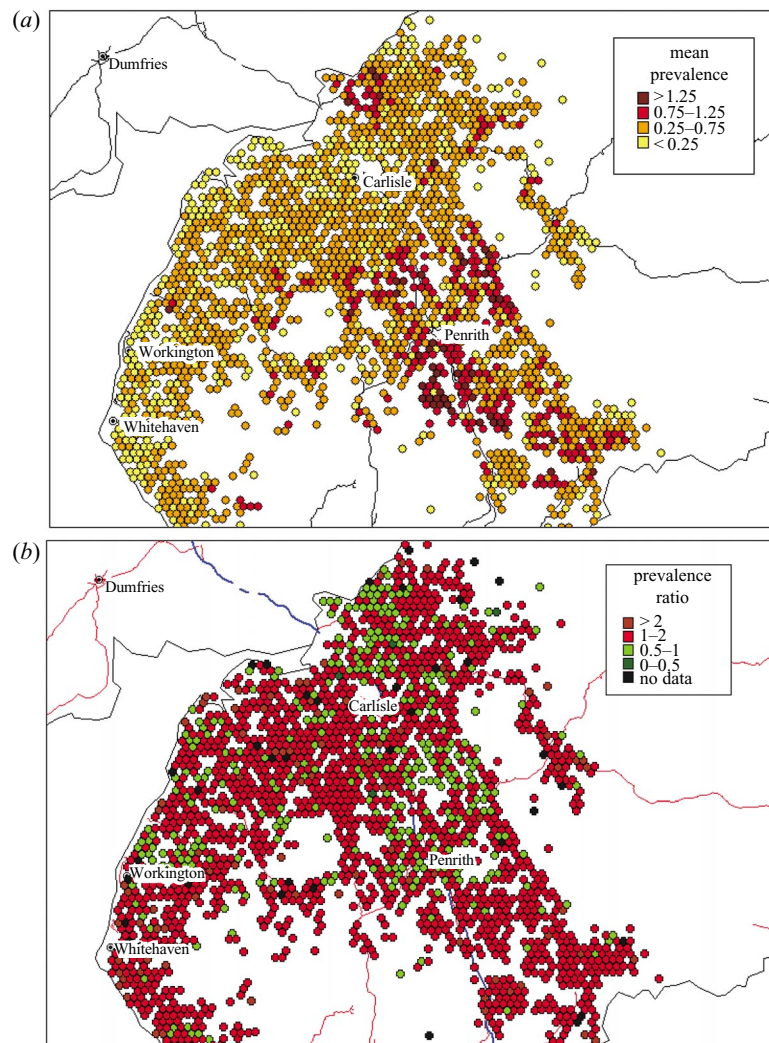
Figure 5. Spatial representation of DC culling, assuming prioritized DC culling from 7 days after movement controls were initiated (2 March). DC culling scenario assumes 20% efficacy prior to 2 March, 100% thereafter, with all CP culls treated as DC culls. (*a*) The average prevalence per hex over 100 simulations for the scenario with prioritized DC culling, and (*b*) the ratio between number of IPs under prioritized DC culling and the number of IPs in the baseline scenario, showing that prioritized DC culling is initially superior (near starting points of the epidemic), but is inferior overall.

factors would be useful, given the logistical resources similar to what was available in 2001. There is still no significant difference between culling policies if the alternative policy is implemented after 23 March, when the decision to prioritize CP culling was announced. Distinct differences in the spatial distribution can be seen by examining the average spatial prevalence distribution over 100 simulations, shown in figure 5*a* for prioritized DC culling from 2 March. The relatively poor performance of prioritized DC culling is emphasized in figure 5*b*, which shows the prevalence ratios under the two policies. In figure 6, the same prevalence ratios are plotted as a function of distance from IP 194. IP 194 was one of the earliest IPs in south east Cumbria (estimated infection date, 21 February) and a major source of the epidemic (estimated total descendants, 230; D. Haydon, personal communication). Although the far north of Cumbria was infected first, this region represents the earliest heavily infected area in Cumbria. Thus, this plot is a crude estimate of the relatively good impact of preferred DC culling early in the epidemic (close to IP 194) and its lesser impact later in the epidemic (far from IP 194).
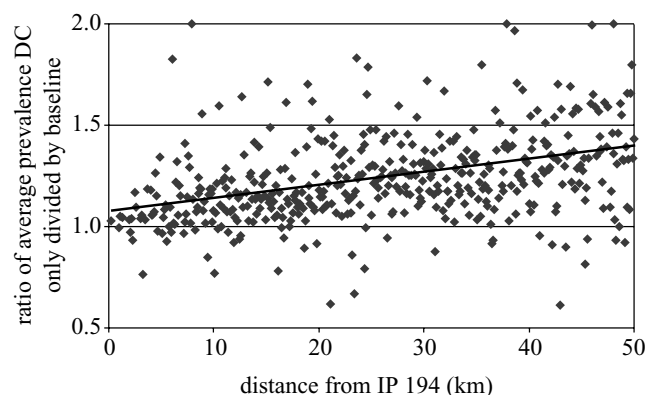

Figure 6. Ratio of expected prevalence by distance from IP 194. This is a crude estimate of the relative impact of preferred DC culling early on in the epidemic (close to IP 194) and later in the epidemic (far from IP 194).
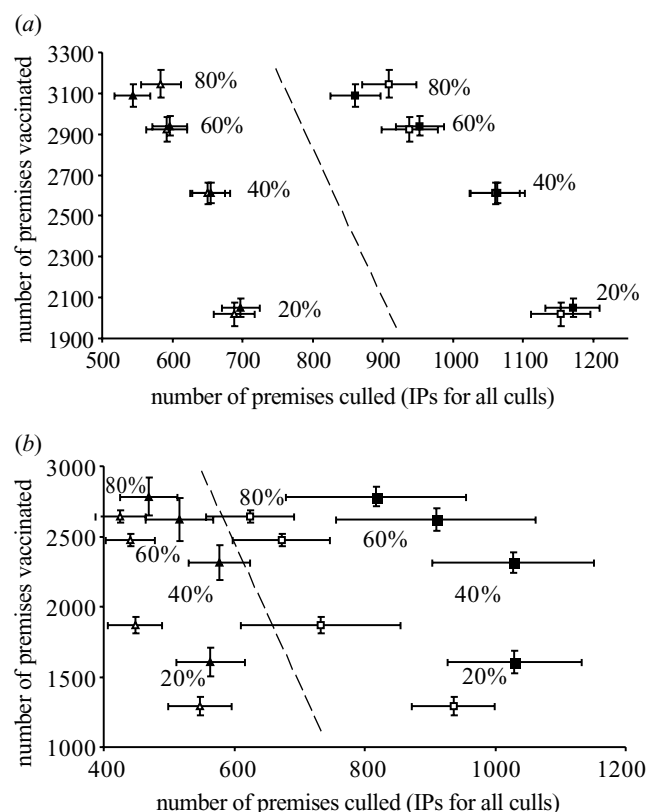
(a)

(b)

Figure 7. Comparison of vaccination policies in Cumbria, implemented 7 days after movement controls were initiated on 23 February. (a) Low variability, (b) high variability. Data series represent increasing coverage of vaccination schemes, indicating 20%, 40%, 60% and 80% coverage of the local neighbourhood to a distance of 3.6 km from the IP triggering the ring vaccination event. Targeting of farms by size and susceptibility is shown in white, targeting of farms by size only is shown in black. Data series to the left of the dashed line (triangles) are the number of IPs versus the number vaccinated; to the right are total culls (squares, IPs plus DCs) versus the number vaccinated. For the best-fit variability in susceptibility ($\sigma = 0.5$, figure 3a), there is no significant difference between the two policies in terms of either the number of IPs or number of culled premises. For greater variability ($\sigma = 1.0$ in figure 3b), there are significant differences in both.

Finally, use of targeting to aid emergency ring vaccination (i.e. vaccination of premises surrounding IPs) is examined. Although such a vaccination policy is superior to the culling in the way that it occurred, again, at the levels of variability most consistent with the Cumbria epidemic, increased knowledge has no apparent effect on a vaccination policy (figure 7a). Should variability be greater than indicated, however (figure 7b, showing differences assuming $\sigma = 1.0$), targeting is potentially valuable. In particular, targeting that includes susceptibility is superior to targeting based on herd size alone at intermediate levels of coverage. This could be important if there are logistical limitations on the amount of vaccine deliverable, as might occur should there be an outbreak of unexpected size, or if the epidemic is caused by an unexpected virus strain that is poorly protected against by existing vaccine stocks. Examining the spatial distribution of IPs and the ratio of IPs under vaccination as compared with the baseline policy (figure 8, showing the distribution

where 60% of premises 3 hexes or less from an IP are vaccinated), the spread of the epidemic is much less than for the baseline scenario, with performance under vaccination inferior earlier in the epidemic, but superior later on (figure 9).

4. DISCUSSION

A prior analysis has shown that the FMD epidemic in Cumbria was probably the only regional outbreak in the 2001 UK epidemic that did not die out owing to local spatial effects (Kao 2001). Outside Cumbria, R_0 was relatively low, and the superior impact of good DC culling in reducing the case reproduction ratio below 1 would probably be important. In Cumbria, however, these simulations indicate that control policy as applied was not working. In this case, the result of varying parameters shows that the interaction of various factors impacting transmission (R_0, the transmission kernel, local variation in susceptibility, global depletion of susceptibles, etc.) is subtle, and the best policy is not easily predicted by straightforward assessment of the risk of contact. In particular, removing the premises that are the most likely to become infected by an IP can be ultimately less effective than a policy that emphasizes local depletion of susceptible premises. This is emphasized in figures 5 and 6, which show that prioritized DC culling initially appears to be superior (i.e. in the regions surrounding earliest IPs), but performs less well as the epidemic expands. Even with a high odds ratio of 3.0, targeting highly susceptible premises is only worthwhile if it can be achieved early on in the epidemic. Indeed, the CP culling policy may be superior even then, because in principle it is simpler to implement and therefore can be applied more rapidly and extensively, factors previously shown to be critical in reducing the epidemic (Ferguson *et al.* 2001*a,b*; Keeling *et al.* 2001; Haydon *et al.* 2003).

The structure of this and earlier models does not allow for analysis of some alternative policies. For example, in the models a herd thinned from 1000 to 100 cattle poses the same risk of transmission as an unthinned herd of 100 cattle. However, it is likely that reducing animal density in non-IPs would offer benefits in improved surveillance and reduced transmission that are not captured under this assumption. There would also be non-epidemiological benefits, such as in regard to animal welfare, genetic diversity preservation and restocking. Farm owners would be able to select their most valuable animals for preservation, drastically reducing compensation (£50 000 in one case for a pedigree ram; National Audit Office 2002). Should this prove popular, it would also be likely to improve farmer compliance and support for the control policy. These benefits are significant, and should be investigated with within-herd transmission models.

While overall agreement with the data is good, there are two discrepancies that need to be addressed: the low incidence in the epidemic tail and differences in the predicted spatial distribution, with more premises infected in regions close to the starting points of the epidemic. The discrepancy in the long epidemic tail may be owing in part to increased transmission rates (Ferguson *et al.* 2001*b*). However, the relative effect of spatial and temporal variation in susceptibility is difficult to determine. In any case,
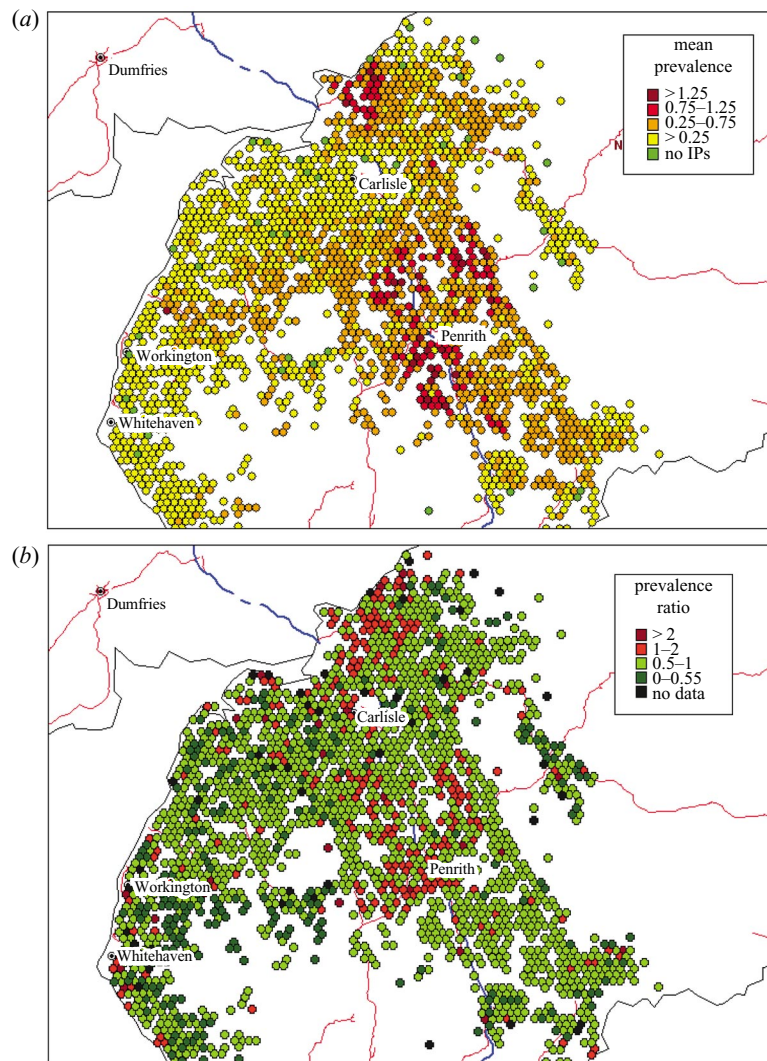
Figure 8. Spatial representation of vaccination, assuming 60% premises coverage from 7 days after movement controls were initiated (2 March). (*a*) The average prevalence per hex over 100 simulations for the prioritized DC culling scenario and (*b*) the ratio between number of IPs under vaccination and the number of IPs in the baseline scenario, showing that the baseline policy is initially superior (near starting points of the epidemic), but is overall inferior.
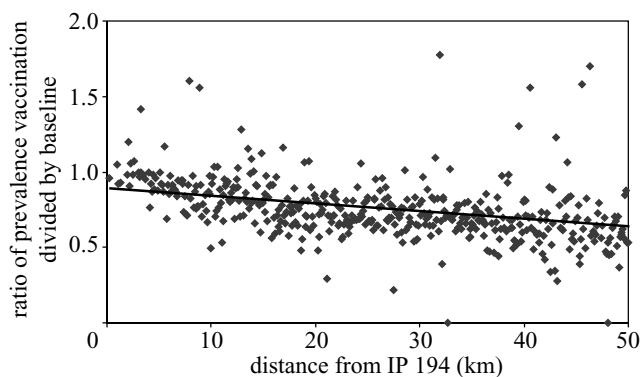

Figure 9. As for figure 6, however, comparing vaccination assuming 60% premises coverage from 7 days after movement controls were initiated (2 March) with the baseline scenario.

the advantages of good DC culling are more pronounced when the reproduction rate is low (it is more likely immediately to reduce the reproduction rate below 1 than CP culling), and thus a low simulated incidence does not

alter the basic conclusion of this analysis. A possible explanation for the spatial discrepancy is systematic differences between the location and numbers of the true animal populations and the census data records (Keeling *et al.* 2001). However, the regions where DC culling is more effective are those afflicted early in the epidemic and before the decision point was made regarding the contiguous cull (figure 5*b*), and thus a better spatial fit is also unlikely to alter the conclusion.

Other difficulties associated with the available data have previously been discussed (Ferguson *et al.* 2001*a,b*; Gibbens *et al.* 2001; Keeling *et al.* 2001; Kao 2002), and the same caveats apply here. In particular, it is difficult to determine the efficacy of control policies based on local investigation (such as DC culling) without knowing 'who is connected to whom', as this can be an important consideration for understanding disease transmission and identifying the most likely targets for disease control (Lloyd & May 2001). Good knowledge of farm demography is absolutely vital to recognizing the types of premises at the highest risk of acquiring and transmitting disease. However, here it is shown that the best decision in a local

decision-making context is not necessarily the best one when viewing the global situation, and that such a global perspective is vital to rapidly establishing the best choice among what often seem to be a plethora of options for disease control.

REFERENCES

Anderson, R. M. & May, R. M. 1992 *Infectious diseases of humans: dynamics and control.* Oxford University Press.

Anon. 2001 Foot and mouth disease: outbreaks exceed 1000. *Vet. Rec.* **148**, 422.

Anon. 2002 Foot-and-mouth disease: RCVS criticises organisation and planning. *Vet. Rec.* **150**, 393–394.

Byrne, D. 2002 A comprehensive EU approach to combating FMD. See http://europa.eu.int/comm/food/fs/ah_pcad/ah_pcad_byrne_en.html.

Cunningham, I. (and 16 others) 2002 *Inquiry into foot-and-mouth disease in Scotland.* Royal Society of Edinburgh.

Doel, T. R. 1999 Optimisation of the immune response to foot-and-mouth disease vaccines. *Vaccine* **17**, 1767–1771.

Ferguson, N. M., Donnelly, C. A. & Anderson, R. M. 2001*a* The foot-and-mouth epidemic in Great Britain: pattern of spread and impact of interventions. *Science* **292**, 1155–1160.

Ferguson, N. M., Donnelly, C. A. & Anderson, R. M. 2001*b* Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. *Nature* **413**, 542–548.

Follett, B. (and 14 others) 2002 *The Royal Society inquiry into infectious diseases in livestock.* London: The Royal Society.

Gibbens, J. C., Sharpe, C. E., Wilesmith, J. W., Mansley, L. M., Michalopoulou, E., Ryan, J. B. & Hudson, M. 2001 Descriptive epidemiology of the 2001 foot-and-mouth disease epidemic in Great Britain: the first five months. *Vet. Rec.* **149**, 729–743.

Gill, I., Lewis, C. & Macaldowie, C. 2002 Modelling and FMD. *Vet. Rec.* **150**, 819.

Haydon, D. T., Chase-Topping, M., Shaw, D. J., Matthews, L., Friar, J. K., Wilesmith, J. & Woolhouse, M. E. 2003 The construction and analysis of epidemic trees with reference to the 2001 UK foot-and-mouth outbreak. *Proc. R. Soc. Lond.* B **270**, 121–127. (DOI 10.1098/rspb.2002.2191.)

Hughes, G. J., Mioulet, V., Kitching, R. P., Woolhouse, M. E., Alexandersen, S. & Donaldson, A. I. 2002 Foot-and-mouth disease virus infection of sheep: implications for diagnosis and control. *Vet. Rec.* **150**, 724–727.

Kao, R. R. 2001 Landscape fragmentation and foot-and-mouth disease transmission. *Vet. Rec.* **148**, 746–747.

Kao, R. R. 2002 The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. *Trends Microbiol.* **10**, 279–286.

Keeling, M. J., Woolhouse, M. E., Shaw, D. J., Matthews, L., Chase-Topping, M., Haydon, D. T., Cornell, S. J., Kappey, J., Wilesmith, J. & Grenfell, B. T. 2001 Dynamics of the 2001 UK foot and mouth epidemic: stochastic dispersal in a heterogeneous landscape. *Science* **294**, 813–817.

Keeling, M. J., Woolhouse, M. E., May, R. M., Davies, G. & Grenfell, B. T. 2003 Modelling vaccination strategies against foot-and-mouth disease. *Nature* **421**, 136–142.

Lloyd, A. L. & May, R. M. 2001 Epidemiology. How viruses spread among computers and people. *Science* **292**, 1316–1317.

National Audit Office 2002 *Report by the Comptroller and Auditor General: the 2001 outbreak of foot and mouth disease.* London: The Stationary Office.

UK Ministry of Agriculture, Fisheries and Foods 2001 *Agricultural and horticultural census.* London: The Stationary Office.

Woolhouse, M. E. J., Haydon, D. T., Pearson, A. & Kitching, R. P. 1996 Failure of vaccination to prevent outbreaks of foot-and-mouth disease. *Epidemiol. Infect.* **116**, 363–371.